REMARKS

Claims were 16, 17, 19-22 and 30-34 were pending in the application. Claim 22 has been canceled, claims 16, 17, 19, 20, 21, 30-34 have been amended and new claims 35-42 have been added. Accordingly, after the amendments presented herein have been entered, claims 16, 17, 19-21 and 30-42 will be pending in the instant application. *No new matter has been added.*

Support for the amendments to the claims and for the new claims can be found throughout the specification and claims as originally filed. In particular, support for the amendments to claim 16 may be found at, for example, in Examples 1, 2, and 3 of Applicants' specification. Support for new claims 35-40 may be found at, for example, in Figure 8 and Example 3 (see, *e.g.*, page 53, lines 22-28) of Applicants' specification.

Cancellation of and/or amendment to the claims should in no way be construed as an acquiescence to any of the Examiner's rejections. The cancellation of and/or amendments to the claims are being made solely to expedite prosecution of the above-identified application. Applicants reserve the option to further prosecute the same or similar claims in the instant or in another patent application.

Information Disclosure Statement

Applicants thank the Examiner for consideration of the references cited in the Information Disclosure Statement filed by Applicants on December 14, 2001. However, Applicants note that the Examiner did not initial From 1449 with respect to references A1-A3 or B1-B5. Applicants' respectfully request that the Examiner consider these references and initial Form 1449 accordingly.

Rejection of Claims 16-17, 19-22, and 30-34 Under 35 U.S.C. 112, First Paragraph

The Examiner has rejected claims 16-17, 19-22, and 30-34 under 35 U.S.C. 112, first paragraph as "failing to comply with the enablement requirement." In particular, the Examiner is of the opinion that:

> the claims require the presence of an IgE fusion protein in the cell, yet the method is directed to identifying an agent that modulates IgE production. Since the IgE is already present it is not clear how the skilled artisan could then measure the effect on IgE production upon the addition of the agent. Secondly, it is not clear to one of skill in the art whether the cell expresses IgE endogenously or whether the only IgE present is that which is in the fusion protein. As such the skilled artisan is not able to practice the method because the method does not set forth whether to measure fluorescence of the fusion protein, or the amount of the endogenously produced IgE. If the method is to measure endogenously produced IgE, the role of the fusion protein in the method is not apparent. If the method is to measure the effect of a bioactive agent on the IL-4 inducible promoter, the claims do not require the presence of a nucleic acid comprising this promoter that encodes a fusion protein comprising the epsilon heavy chain and a fluorescent protein.

Applicants respectfully submit that one of ordinary skill in the art would be able to make and use the claimed invention without undue experimentation for the following reasons. Claim 16, as amended, is directed to a method of screening for a bioactive agent that modulates IgE production, the method comprising contacting, under conditions permissive for expression of an IgE fusion protein, a candidate bioactive agent and a cell, the cell comprising a genome which has been modified to express an IgE fusion protein under the control of an IgE promoter, the IgE fusion protein comprising: an ε heavy chain; and a fluorescent protein, and determining the amount of the IgE fusion protein expressed by the cell; wherein a difference in the amount of the IgE fusion protein expressed in the presence of the candidate agent as compared to the amount

expressed in the absence of the candidate agent indicates that the agent modulates IgE production.

Applicants' respectfully submit that claim 16 specifically requires that the genome of the cell is modified to express an IgE fusion protein. The claim also requires determining the ***difference in the amount of IgE fusion protein expressed in the presence of the candidate agent as compared to the amount expressed in the absence of the candidate agent.*** Accordingly, the claim clearly requires measuring expression of the IgE fusion protein as an indicator of the ability of the candidate bioactive agent to affect IgE expression. The difference in the amount of IgE fusion protein expressed may be determined using techniques well-known to one of ordinary skill in the art. Claim 40 is specifically directed to measuring expression of the fluorescent protein.

Therefore, it is Applicants' position that, given the guidance in Applicants' specification and the teachings in the art at the time the invention was made, one of ordinary skill in the art would be able to practice the invention as claimed to identify bioactive agents that modulate IgE production, using no more than routine experimentation. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

Rejection of Claims 16-17, 19-22, and 30-34 Under 35 U.S.C. 112, Second Paragraph

The Examiner has rejected claims 16-17, 19-22, and 30-34 under 35 U.S.C. 112, second paragraph as "failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." In particular, the Examiner is of the opinion that

> it is not clear whether the cell expresses IgE endogenously, or whether the IgE fusion protein itself meets the limitation that the cell expresses IgE. Furthermore, as set forth *supra,* it is not clear how the method would

> detect an effect on IgE production, since the production of IgE is not necessarily dependent on the presence of the fusion protein, and further, the fusion protein is not, e.g. encoded by a nucleic acid comprising an inducible promoter. Furthermore, the method does not set forth that the IgE produced is determined by measuring the fluorescent protein, only by measuring IgE, thus the presence of the fusion protein would seem to have no role in the method as written.

Applicants respectfully traverse the foregoing rejection and submit that claims 16-17, 19-22, 30-34 are clear and definite. Applicants respectfully submit that claim 16, as amended, recites that the cell used in the methods of the invention is capable of expressing IgE and ***is modified to express an IgE fusion protein***. Furthermore, the detection of an effect on expression of the IgE fusion protein by the candidate bioactive agent is determined by measuring the difference in expression of the fusion protein by the cell in the presence of the candidate agent as compared to expression of the fusion protein in the absence of the candidate agent. The ability of the candidate bioactive agent to modulate expression of the IgE fusion protein is used as an indicator of the ability of the agent to modulate IgE expression in a cell. The claims clearly set forth the steps for identifying a bioactive agent that modulates IgE production.

Therefore, for the reasons set forth above, claim 16 is clear and definite and would be understood by one of ordinary skill in the art when read in combination with the teachings of the specification taken as a whole. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

CONCLUSION

If a telephone conversation with Applicants' Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,

LAHIVE & COCKFIELD, LLP

By: _____
Megan E. Williams, Esq.
Registration No. 43,270
Attorney for Applicants

28 State Street
Boston, MA 02109
(617) 227-7400
(617) 742-4214

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